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Applicants : Philip O. Livingston et al.

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Serial No 08/477,097

Group-Art Unit GROUP 3500

Filed June 7, 1995

For GANGLIOSIDE-KLH CONJUGATE VACCINES PLUS QS-21



1185 Avenue of the Americas  
New York, New York 10036  
December 11, 1995

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

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In compliance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references, which are listed on the accompanying form PTO-1449 (Exhibit 1), copies of which are attached hereto as Exhibits 2-14, respectively:

1. Irie R.F. et al., U.S. Patent No. 4,557,931, issued December 10, 1985 from U.S. Serial No. 446,231, filed December 2, 1982 (Exhibit 2);
2. Livingston P.O. et al., U.S. Patent No. 5,102,663, issued April 7, 1992 from U.S. Serial No. 259,182, filed October 18, 1988 (Exhibit 3);
3. Fung P.Y.S. et al., "Active Specific Immunotherapy of a Murine Mammary Adenocarcinoma Using a Synthetic Tumor-associated Glycoconjugate" Cancer Research, July 15, 1990, Vol. 50, pages 4308-4314 (Exhibit 4);

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4. Kensil R.C. et al., "Separation and Characterization of Saponins with Adjuvant Activity from *Quillaja Saponaria* Molina Cortex", The Journal of Immunology, January 15, 1991, Vol. 146, No. 2, pages 431-437 (Exhibit 5);
5. Livingston P.O. et al., "Characterization of IgG and IgM Antibodies Induced in Melanoma Patients by Immunization with Purified G<sub>M2</sub> Ganglioside", Cancer Research, December 15, 1989, Vol. 49, pages 7045-7050 (Exhibit 6);
6. Livingston P.O. et al., "Studies of the Immunogenicity of Synthetic and Natural Thomsen-Friedenreich (TF) Antigens in Mice: Augmentation of the Response by Quil A and SAF-m Adjuvants and Analysis of the Specificity of the Responses, Vaccine Research, Vol. 1, No. 2, 1992, pages 99-109 (Exhibit 7);
7. MacLean G.D. et al., "Immunization of Breast Cancer Patients Using a Synthetic Sialyl-Tn Glycoconjugate Plus Detox Adjuvant", Cancer Immunol. Immunother., Vol. 36, 1993, pages 215-222 (Exhibit 8);
8. MacLean G.D. et al., "Active Immunization of Human Ovarian Cancer Patients Against a Common Carcinoma (Thomsen-Friedenreich) Determinant Using a Synthetic Carbohydrate Antigen", Journal of Immunotherapy, Vol. 11, 1992, pages 292-305 (Exhibit 9);
9. Marciani D.J. et al., "Genetically-engineered Subunit Vaccine Against Feline Leukaemia Virus: Protective Immune Response in Cats", Vaccine, Vol. 9, February 1991, pages 89-96 (Exhibit 10);

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10. Newman J.M. et al., "Saponin Adjuvant Induction of Ovalbumin-Specific CD8<sup>+</sup> Cytotoxic T Lymphocyte Responses", The Journal of Immunology, Vol. 148, No. 8, April 15, 1992, pages 2357-2362 (Exhibit 11);
11. Ritter G. et al., "Ganglioside Antigens Expressed by Human Cancer Cells", Seminars in Cancer Biology, Vol 2, 1991, pages 401-409 (Exhibit 12);
12. Ritter G. et al., "Antibody Response to Immunization with Purified GD3 Ganglioside and GD3 Derivatives (Lactones, Amide and Gangliosidol) in the Mouse", Immunobiol., 1990, Vol. 182, pages 32-43 (Exhibit 13);
13. Wu J-Y. et al., "Saponin Adjuvant Enhancement of Antigen-Specific Immune Responses to an Experimental HIV-1 Vaccine", The Journal of Immunology, Vol. 148, 1992, pages 1519-1525 (Exhibit 14);

Irie R.F. et al., Patent No. 4,557,931 (Exhibit 2) discloses the Immunogenicity of the ganglioside GM2 present at the surface of the tumor cells.

Livingston P.O. et al., Patent No. 5,102,663 (Exhibit 3) discloses a vaccine for stimulating production of antibodies directed against 9-O-Acetyl GD3 ganglioside.

Fung P.Y.S. et al., (Exhibit 4) disclose a synthetic tumor-associated glycoconjugate (S-TAG) vaccine effective against a murine mammary adenocarcinoma (TA3-HA).

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Kensil R.C., et al., (Exhibit 5) disclose the purification of Saponins from *Quillaja saponaria* and their utilizations as adjuvant in mouse immunization.

Livingston P.O. et al. (Exhibit 6) disclose the induction of IgG and IgM antibodies to immunization with G<sub>M2</sub> ganglioside in Melanoma patients.

Livingston P.O. et al. (Exhibit 7) disclose the effect of Quil A and SAF-m adjuvant on the immunogenicity in mice.

MacLean G.D. et al. (Exhibit 8) disclose the antibody response to immunization with a synthetic sialyl-Tn glycoconjugate plus Detox adjuvant.

MacLean G.D. et al. (Exhibit 9) disclose the antibody response to immunization with Thomsen-Friedenreich antigen conjugated to KLH plus Detox adjuvant.

Marciani D.J. et al. (Exhibit 10) disclose the antibody response to immunization with a genetically-engineered subunit vaccine in cats.

Newman M.J. et al. (Exhibit 11) disclose the QS-21 Saponin adjuvant induction of Ovalbumin-Specific CD8<sup>+</sup> cytotoxic T lymphocyte responses.

Ritter G. et al. (Exhibit 12) review the ganglioside expressed on the human cancer cells and disclose their utilizations in immunotherapy.

Ritter G. et al. (Exhibit 13) disclose methods to increase the immunogenicity of GD3 ganglioside.

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Wu J.Y. et al. (Exhibit 14) disclose the use of Saponin as adjuvant to an experimental HIV-1 vaccine.

Applicants also attach as Exhibit 15 a copy of the PCT Search Report for PCT Application No. PCT/US94/00757, filed January 21, 1994 with the U.S. Receiving Office.

In view of the preceding remarks, applicants maintain that none of the above-listed references disclose or suggest the invention claimed in the subject application.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicants undersigned attorney invites the Examiner to telephone at the number provided below.

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No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required in connection with the filing of this Information Disclosure Statement, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Albert Wai Kit Chan

I hereby certify that this paper is being deposited this date with the U.S. Postal Service as first class mail addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Albert Wai Kit Chan 6/7/95  
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